Human Research Protection Program: Institutional Official Training

Defense Health Agency Office of Research Protections

18 March 2021

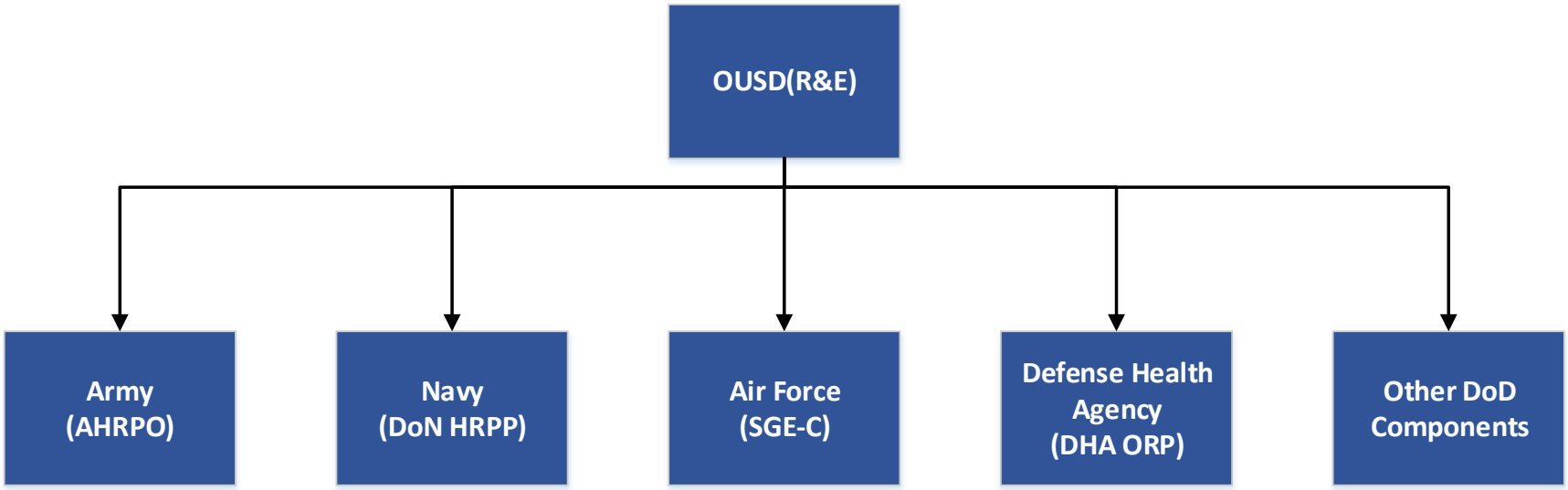
"Medically Ready Force…Ready Medical Force"

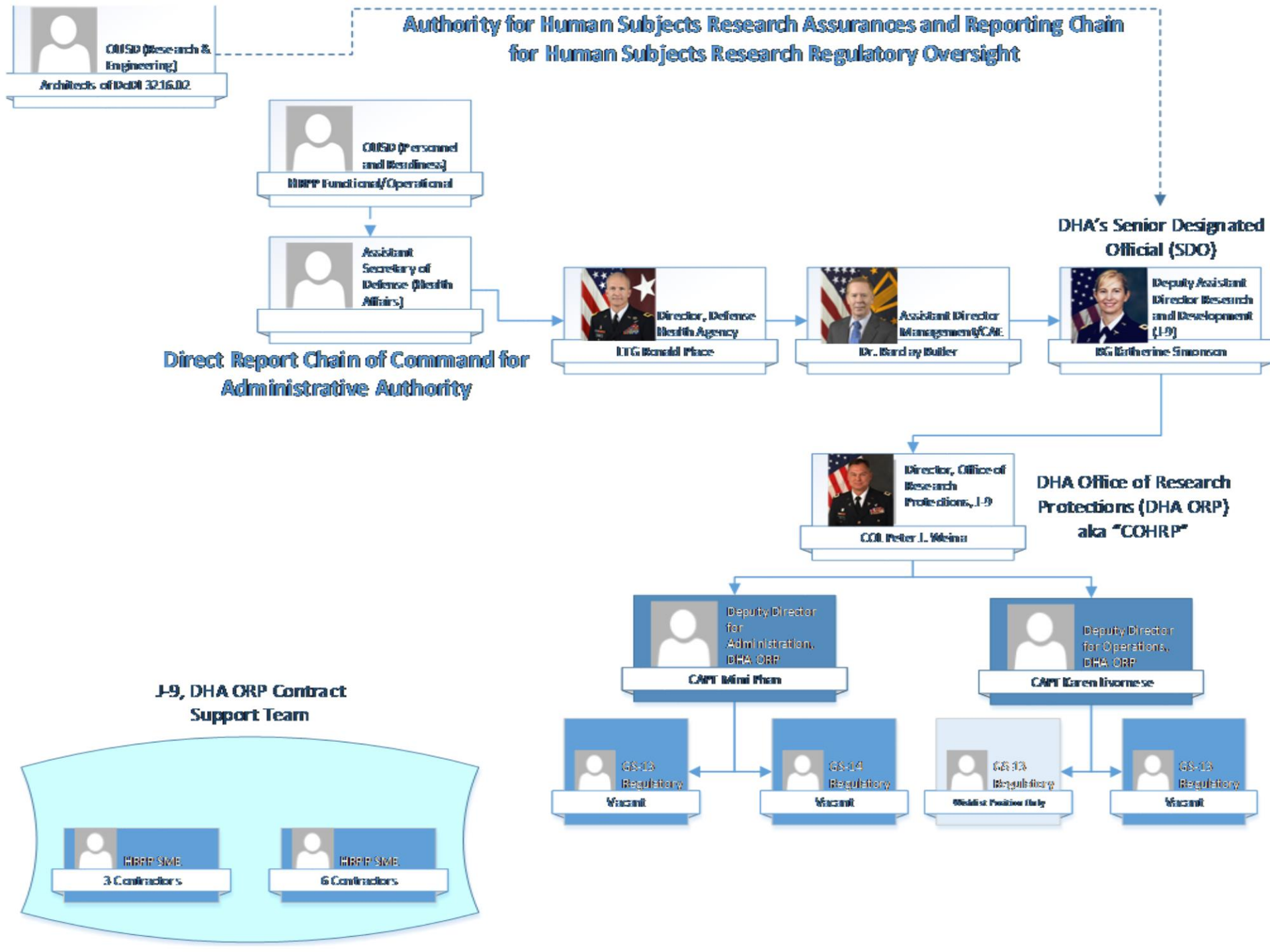
Goals of Training

- Provide an Overview of the HRPP
- Explain the role of the Institutional Official
- Human Subjects Research
- Human Subjects Research conducted at your institution
- How the research conducted at your institution impacts the role of the IO

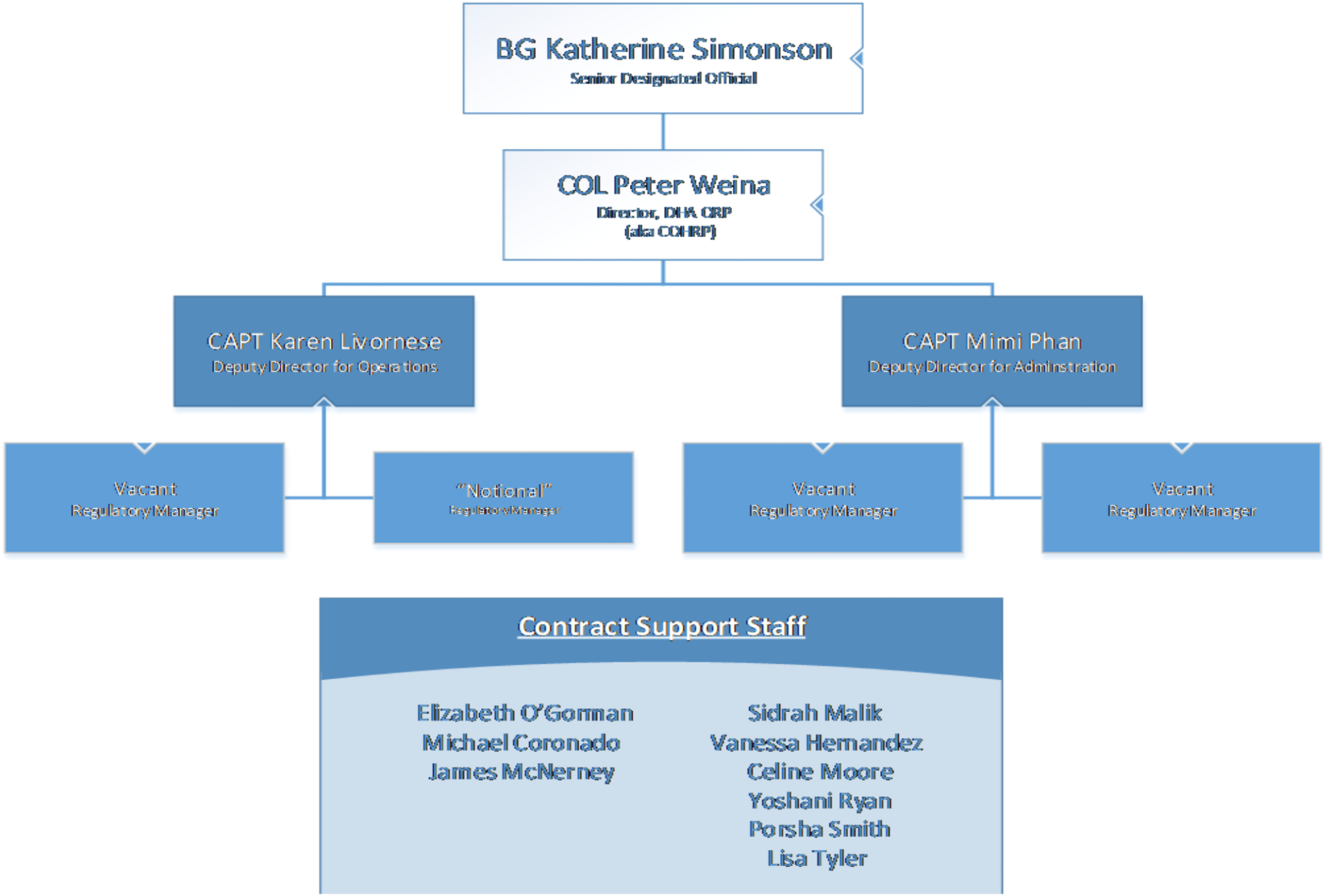
Human Research Protections Program (HRPP) Overview

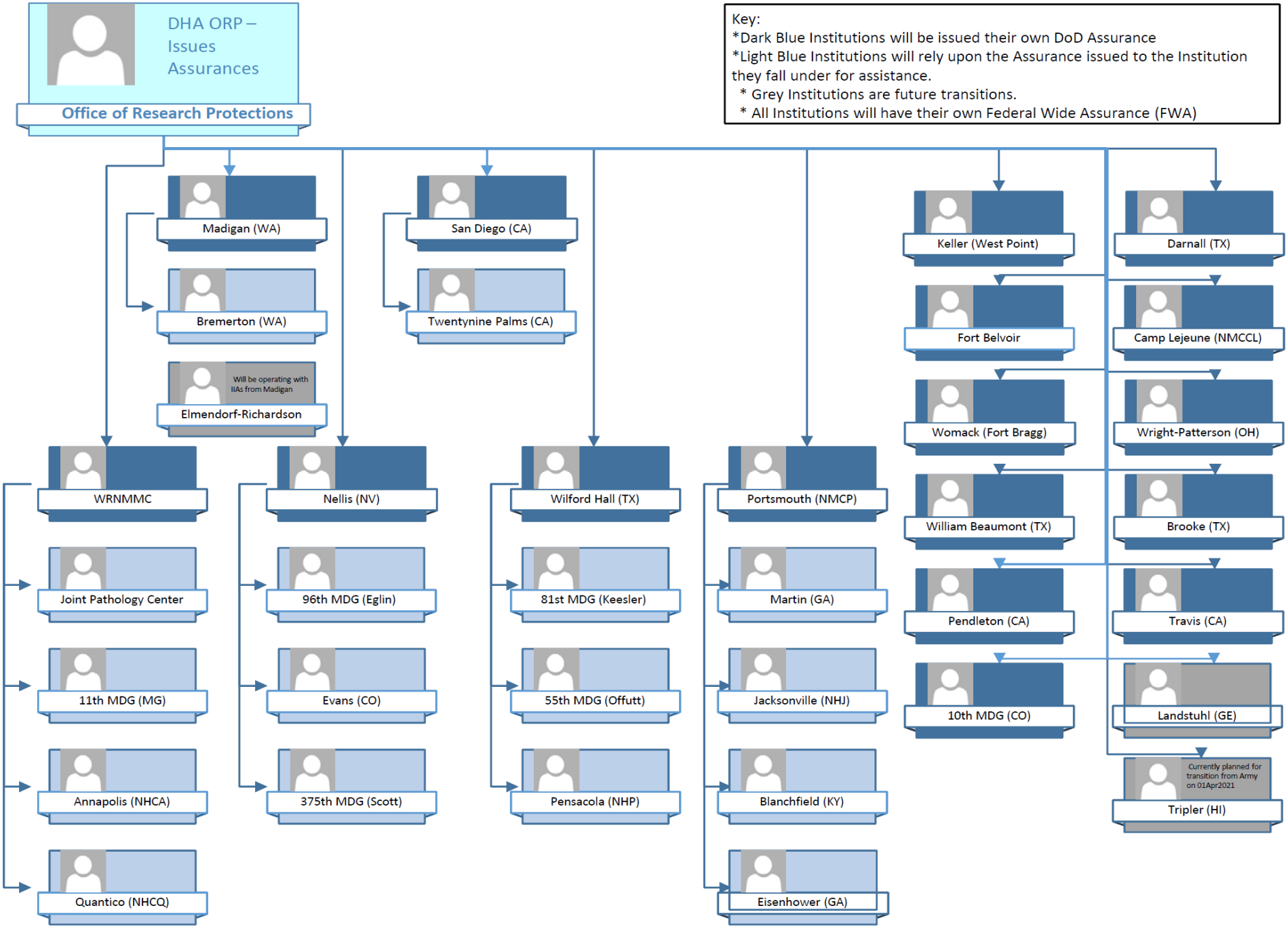
DoD HRPP Overview



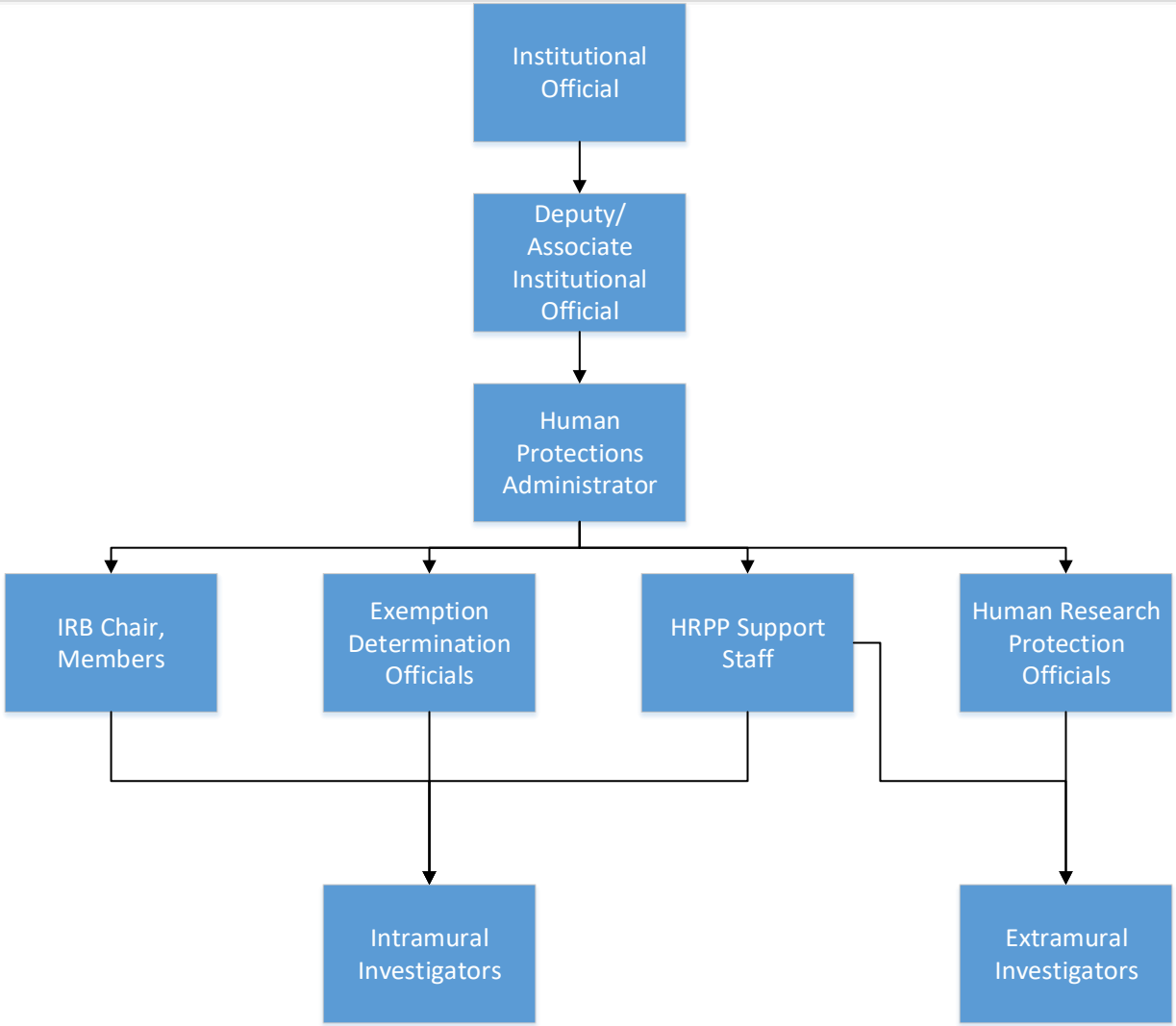

Authority for Human Subjects Research Assurances and Reporting Chain for Human Subjects Research Regulatory Oversight
OUSD (Research & Engineering)
Architects of DoDI 3216.02
OUSD (Personnel and Readiness)
HRPP Functional/Operational
Assistant Secretary of Defense (Health Affairs)
Direct Report Chain of Command for Administrative Authority
Director, Defense Health Agency
LTG Ronald Place
Assistant Director Management/CAE
Dr. Barclay Butler
DHA's Senior Designated Official (SDO)
Deputy Assistant Director Research and Development (J-9)
BG Katherine Simonson
Director, Office of Research Protections, J-9
COL Peter L. Weina
DHA Office of Research Protections (DHA ORP) aka "COHRP"
Deputy Director for Administration, DHA ORP
CAPT Mimi Phan
Deputy Director for Operations, DHA ORP
CAPT Karen Ivornese
GS-13 Regulatory
Vacant
GS-14 Regulatory
Vacant
GS-13 Regulatory
Waitlist Position Only
GS-13 Regulatory
Vacant
J-9, DHA ORP Contract Support Team
HRPP SME
3 Contractors
HRPP SME
6 Contractors

Defense Health Agency Office of Research Protections

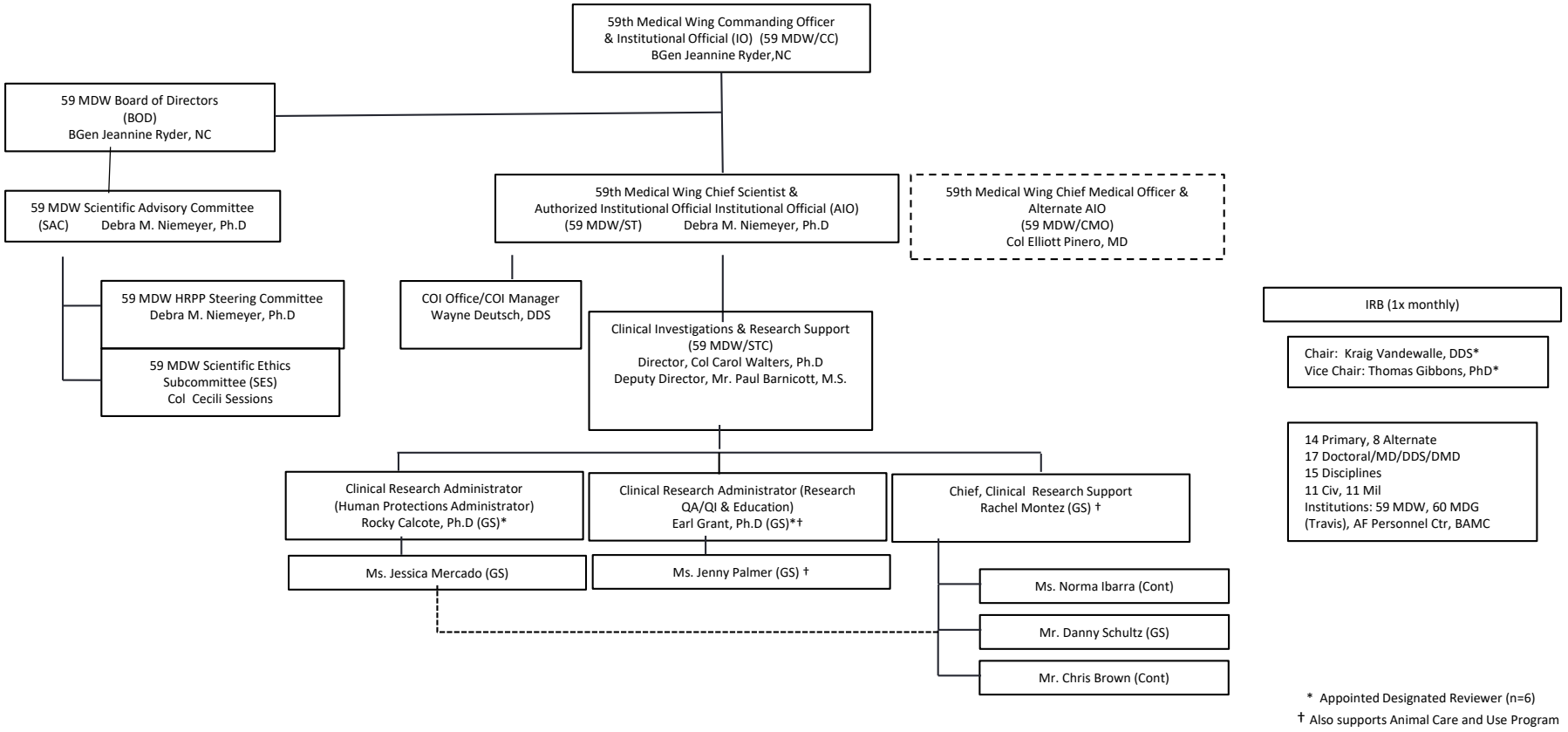



DHA ORP – Issues Assurances
Office of Research Protections
Key:
*Dark Blue Institutions will be issued their own DoD Assurance
*Light Blue Institutions will rely upon the Assurance issued to the Institution they fall under for assistance.
* Grey Institutions are future transitions.
* All Institutions will have their own Federal Wide Assurance (FWA)
Madigan (WA)
Bremerton (WA)
Elmendorf-Richardson
Will be operating with IIAs from Madigan
San Diego (CA)
Twentynine Palms (CA)
Keller (West Point)
Fort Belvoir
Womack (Fort Bragg)
William Beaumont (TX)
Pendleton (CA)
10th MDG (CO)
Darnall (TX)
Camp Lejeune (NMCCL)
Wright-Patterson (OH)
Brooke (TX)
Travis (CA)
Landstuhl (GE)
Tripler (HI)
Currently planned for transition from Army on 01Apr2021
WRNMMC
Joint Pathology Center
11th MDG (MG)
Annapolis (NHCA)
Quantico (NHCQ)
Nellis (NV)
96th MDG (Eglin)
Evans (CO)
375th MDG (Scott)
Wilford Hall (TX)
81st MDG (Keesler)
55th MDG (Offutt)
Pensacola (NHP)
Portsmouth (NMCP)
Martin (GA)
Jacksonville (NHJ)
Blanchfield (KY)
Eisenhower (GA)

HRPP Overview - Institution



59 MDW HRPP



* Appointed Designated Reviewer (n=6)

† Also supports Animal Care and Use Program

"Medically Ready Force…Ready Medical Force"

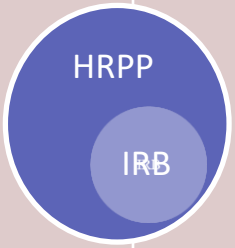
HRPPs vs. IRBs: Constitution and Membership

HRPP	IRB
DoD HRPPs include: • The Institutional Official • The HPA/HPD • EDO(s) • HRPO(s) • Investigators and Research Team Members • Research Monitors, if appointed by the IRB • Ombudspersons • IRB(s) • HRPP and IRB Support Staff • Include Federal Employees, Service Members, and Contractors	DoD IRBs include: • At least 5 members, with varying backgrounds • At least one member whose primary concerns are in scientific areas • At least one member whose primary concerns are in nonscientific areas • At least one member who is not otherwise affiliated with the institution and at least one alternate for the non-affiliated member • All voting members must be Federal employees or Service members

HRPPs vs. IRBs: Responsibility and Authority

HRPP	IRB

• A program within an institution that provides the essential support for human research being conducted or supported by that institution
• Develop policies and procedures related to human subjects research oversight and/or implements the Component HRPP's policies and procedures
• May or may not support an IRB depending on the structure of the institution
• An IRB is a part of and will always fall under an HRPP
	• Review non-exempt human subjects research and make decisions regarding:
	  • Risks to subjects are minimized
	  • Risks-to-potential benefits ratio
	  • Informed consent
	  • Selection of subjects
	  • Data monitoring
	  • Privacy of subjects
	  • Confidentiality of data
	  • Additional safeguards to protect the rights and welfare of vulnerable subjects, when applicable
	• May be internal or external to the institution conducting research



Role of the Institutional Official (IO)

Institutional Official: Role

- Establish and maintain the institution's HRPP, including an Assurance if appropriate
- Establish procedures to:
  - ❑ Evaluate and improve the HRPP
  - ❑ Ensure personnel receive HRPP training
  - ❑ Ensure activities receive appropriate HRPP reviews
  - ❑ Ensure personnel conducting HRPP reviews do so IAW applicable regulations, policies, & procedures
  - ❑ Ensure scientific reviews of non-exempt research are conducted and the findings are available for consideration by the IRB
  - ❑ Eliminate duplicative ethical/regulatory reviews for collaborative research

Institutional Official: Role, cont.

- Identify an IRB to conduct Limited IRB reviews and reviews of non-exempt research
- Appoint HRPP Personnel:
  - Human Protections Administrator (HPA)
  - Exemption Determination Official(s) (EDO)
  - Human Research Protection Official(s) (HRPO)
  - Institutional Review Board (IRB) Chair and Members
- Approve or disapprove research involving human subjects to be conducted at the institution, as follows:
  - IO may NOT approve research that has been disapproved by the IRB
  - IO may disapprove research that has been approved by the IRB

Deputy/Associate IO

- The IO may formally delegate the authority to perform specified duties to senior officials within the institution
- Delegation of authority for particular duties does not divest the IO of the responsibility to implement and maintain the institution's HRPP
- Delegation of duties and authorities must be in writing

Deputy/Alternate IO: Role

- Perform the duties and authorities specified in the formal appointment memorandum
- Serve as the Acting IO in the absence of the IO
- Delegate authorities and responsibilities as needed to another senior official/leader within the institution

Human Subjects Research

Human Subjects Research Topics

- Ethical Principles and HRPP Requirements
  - Belmont Report – Ethical Principles
  - 32 CFR 219 – Regulatory Requirements
  - DoD Instruction 3216.02 – DoD Requirements
- Defining Human Subjects Research
- Applying Exemptions
- Identifying and Mitigating Conflicts of Interest

The Belmont Report – Ethical Principles

- Published in 1979
- Ethical principles and guidelines for the protection of human subjects in research
- Report is separated into 3 sections:
  - Boundaries between Practice and Research
  - Basic Ethical Principles
    - Respect for Persons
    - Beneficence
    - Justice
  - Applications (of the ethical principles)

32 CFR 219 – Regulatory Requirements

- Implements the principles and applications of the Belmont Report
- DoD codification of the Common Rule
- Identical regulation formally adopted by 15 Federal departments and agencies

DoDI 3216.02 – DoD Requirements

- Implements the Common Rule for DoD
- DoD Institutions conducting non-exempt research must have a DoD-issued Assurance
- DoD Institutions conducting human subjects research must have procedures for making appropriate regulatory determinations, including training personnel
- DoD Institutions must have policies and procedures requiring consideration of scientific merit of non-exempt research
- DoD Institutions must have policies and procedures to ensure human subjects research has been approved by all required organizations before subjects are recruited or other research activities with human subjects begin

Defining Human Subjects Research

Research - A systematic investigation, including research development, testing and evaluation (RDT&E), designed to develop or contribute to generalizable knowledge

- Activities that meet this definition constitute research for the purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities
- Applicability of the definition of research is not dependent on the budget activities funding the research, the mission of the DoD organization conducting or supporting the research, the security classification of the research, the location of the research in the United States or a foreign country, or whether the research is conducted or supported under a program that is not considered research for other purposes

Defining Human Subjects Research, cont

For the purposes of 32 CFR 219, the following activities are deemed NOT to be research:

1. Scholarly and journalistic activities, including the collection and use of information, that focus directly on the specific individuals about whom the information is collected
2. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority
3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes
4. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions

Defining Human Subjects Research, cont

Human Subject - A living individual about whom an investigator (whether professional or student) conducting research:

1. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens, or
2. Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens

- Human Subjects Research is "research" that involves "human subjects"
- An appropriately trained HRPP Official must review and determine whether activities meet the definition of human subjects research

DoDI Excluded Activities (DoDI 3216.02)

For the purposes of DoD conducted or supported research, the following activities are NOT considered human subjects research:

1. Activities carried out solely for purposes of diagnosis, treatment, or prevention of injury and disease under force health protection programs of DoD, including health surveillance pursuant to Section 1074f of Title 10, U.S.C., and the use of medical products consistent with DoDI 6200.02.
2. Health and medical activities as part of the reasonable practice of medicine or other health professions undertaken for the sole purpose of diagnosis, cure, mitigation, treatment, or prevention of disease in a patient.
3. Activities performed for the sole purpose of medical quality assurance.

DoDI Excluded Activities (DoDI 3216.02), cont

4. Activities that meet the definition of operational test and evaluation as defined in Section 139(a)(2)(A) of Title 10, U.S.C.
5. Activities performed solely for assessing compliance, including occupational drug testing, occupational health and safety reviews, network monitoring, and monitoring for compliance with requirements for protection of classified information.
6. Activities, including program evaluation and surveys, user surveys, outcome reviews, and other methods, designed solely to assess the performance of DoD programs where the results are only for the use of government officials responsible for the operation or oversight of the program being evaluated.

Applying Exemptions

- 32 CFR 219 lists 8 categories of activities that ARE considered human subjects research but are EXEMPT from the regulatory requirements
  - ❑ Exempt research is NOT exempt from applying the principles of the Belmont Report
  - ❑ Exempt research is NOT exempt from all provisions of DoDI 3216.02
  - ❑ Exemption determinations must only be made by an appropriately authorized and trained HRPP official
  - ❑ Human Subjects Research that does not meet any of the 8 categories (i.e., non-exempt research) must be reviewed and approved by an IRB

Timing of Reviews

- All HRPP reviews (Determinations and IRB) must be completed before any proposed activities may begin

- The HRPP might receive requests to review projects that are underway and/or have been completed. Such retrospective reviews are NOT permitted.

Conflicts of Interest

Actual or Potential Conflicts of Interest

- Individuals' interests that do, or may, conflict with their interests in appropriately protecting human subjects from risk due to the subjects' participation in research include:
  - ❑ Financial Interests
  - ❑ Professional Interests
  - ❑ Familial Interests
  - ❑ Other Interests

- All actual/potential conflicts of interest described are applicable to both investigators and reviewers

Significant Financial Interests

- When an individual or their immediate family receive, in aggregate, over a 12-month period:
  - ❑ Compensation that could be affected by the study outcome
  - ❑ A proprietary interest in the tested product (e.g., patent, trademark, licensing agreement, right to royalties)
  - ❑ Any equity interest in the sponsor or product (e.g., ownership interest, stock options)
    - Of value that cannot be readily determined
    - That exceeds $10,000 (DHA) or 5% ownership interest (59 MDW limit is $5,000)
  - ❑ Significant payments or other compensation with a cumulative value of $10,000 (e.g., research or educational grant, equipment, honorarium) (59 MDW limit is $5,000)

Professional Interests

- Investigators may experience institutional or other professional pressure to publish findings or otherwise prioritize outcomes over the protection of human subjects
- Reviewers may experience actual or perceived pressure to approve particular research because the topic is of interest to Leadership, or because the investigator is a supervisor, subordinate, or high ranking official
- Investigators or reviewers who perform multiple roles (e.g., investigator who is also a clinician and a lecturer) may not be able to devote sufficient time to protecting human subjects in their research

Familial and Other Interests

- Familial Interests:
  - Investigators typically experience familial interests through family members' financial interests
  - Reviewers are likely to experience familial interests through family members' professional interests in a study (e.g., being asked to review a protocol on which a family member is an investigator)
- Other interests
  - Interests that drive people to act are not limited to financial, professional, and familial interests
  - Consideration of conflicts of interest should not be limited to those explicitly described here

Managing Conflicts of Interest: Investigators

- Investigators are responsible for disclosing any actual or potential conflicts of interest at the time the activity is submitted for HRPP review, when a new conflict arises and re-affirmed annually
- Investigators who have identified (and disclosed) an actual or potential conflict of interest must propose a management strategy
- Appropriate management depends on both the nature of the conflict and the nature of the research – strategies listed here are only examples:
  - ❑ Disclosure of the conflict of interest to potential subjects during the informed consent process
  - ❑ The conflicted individual does not participate in certain aspects of the research (e.g., recruitment, consent, data analysis)

Managing Conflicts of Interest: Reviewers

- Reviewers are responsible for disclosing any actual or potential conflicts of interest with a proposed activity as soon as possible after the conflict is identified
- HRPP Reviewers are not permitted to make determinations about protocols with which they have an actual or potential conflict of interest:
  - They MAY participate in initial discussions about the protocols, acting as expert consultants to the reviewer(s) who will make the formal determination
  - They MAY NOT participate in or be present for the determination made about the protocols
    - For example: An IRB member with a conflict of interest may participate in the initial deliberation and answer questions about a protocol, but must recuse themselves and leave the meeting room prior to the final deliberation and vote on the protocol

Questions?

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[rocky.d.calcote.civ@mail.mil]

Contact DHA ORP at

dha.hrpp@mail.mil

Supplemental Slides

IO Authorities that MAY be Delegated

1. Draft institutional HRPP and implementing policies/procedures
2. Regularly review and update HRPP documents
3. Develop HRPP manning document, staffing plan
4. Provide sufficient space for HRPP personnel
5. Provide sufficient IT for the HRPP and HRPP personnel
6. Ensure initial and ongoing HRPP training opportunities for HRPP personnel
7. Engage in HRPP hiring actions
8. Commit funds to support the HRPP infrastructure
9. Approve Individual Investigator Agreements
10. Approve Institutional Agreements for IRB Review
11. Report changes in HRPP Officials and IRB roster to DHAP ORP
12. Require the IRB to investigate allegations of serious or continuing noncompliance, SAEs and UPIRTSOs

IO Authorities that MAY NOT be Delegated

1. Review and sign the Assurance on behalf of the institutions covered by the Assurance
2. Review and be responsible for the institution's FWA if the institution is engaged in research supported by DHHS

Belmont Report Section A: Boundaries between Practice and Research

Practice

Interventions to *enhance* the well-being of an individual that has a reasonable chance for success

Research

Designed to *test* an hypothesis and develop/contribute to generalizable knowledge

Belmont Report Section B: Basic Ethical Principles

Respect for Persons	Beneficence	Justice
• Autonomy: respect peoples' ability to make their own decisions • People with diminished autonomy should have special protections	• Do no harm • Maximize possible benefits and minimize possible harms	• Fairness in Distribution • Equality among people who receive benefits and those who bear burdens

Belmont Report Section C: Applications

Respect for Persons: Informed Consent

- Information – Disclosure of relevant information prior to and during subjects' participation in research
- Comprehension – Information should be presented in a way that is comprehensible to the subject
- Voluntariness – No undue influence or coercion for the subject

Beneficence: Assessment of Risks and Benefits

- Nature and Scope of Risks – The risks considered should include all types of risks related to the subjects' participation in the research (not only physical), as well as potential loss of benefits
- Assessment of Risks and Benefits – Should be a systematic and non-arbitrary assessment of the risk-to-benefit ratio

Justice: Selection of Subjects

- Social Justice – Equitable distribution of benefits and burdens of research across populations, protections for vulnerable populations
- Individual Justice – Selection or non-selection of individual subjects, protections for vulnerable subjects

32 CFR 219

- Implements Respect for Persons
  - Requires that informed consent be obtained from each subject or the subject's representative
  - Requires that informed consent be documented
  - Requires additional protections for individuals unable to provide consent and who are vulnerable to coercion and undue influence
- Implements Beneficence
  - Requires that risks are minimized and reasonable in relation to the anticipated benefits
  - Requires review by a convened IRB for research that is greater than minimal risk
- Implements Justice
  - Requires equitable selection of subjects

DoDI 3216.02 - DoD Requirements

- Implements Respect for Persons
  - Requires additional protections for populations potentially vulnerable to coercion and/or undue inducement
- Implements Beneficence
  - Clarifies and interprets 32 CFR 219 definition of "minimal risk" to protect classes of subjects who encounter increased risk in their daily life due to their work environment or a medical condition
- Implements Justice
  - Requires equitable selection of subjects, including gender and minority participation

Exemption Category 1

Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices *that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction.* This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exemption Category 2

Research that *only includes interactions* involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; *or*

Exemption Category 2 (continued)

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review.

Note:

- The restriction on the inclusion of children only in observations of public behavior is retained in the 2018 Requirements
- Limited IRB Review will be discussed in a subsequent targeted training

Exemption Category 3

Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

Exemption Category 3 (continued)

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review.

Exemption Category 3 (continued)

- Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.
- If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

Exemption Category 4

Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to subjects, *the investigator does not contact the subjects, and the investigator will not re-identify subjects*;

Exemption Category 4 (continued)

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with applicable federal privacy standards found in the E-Government Act, Privacy Act and the Paperwork Reduction Act.

Exemption Category 5

Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

Exemption Category 5 (continued)

- Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.
- Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

Exemption Category 6

Taste and food quality evaluation and consumer acceptance studies:

(i) If wholesome foods without additives are consumed, or

(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Exemption Category 7

Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §219.111(a)(8)

Exemption Category 8

Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

(i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §219.116(a)(1) through (4), (a)(6), and (d);

(ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §219.117;

(iii) An IRB conducts a limited IRB review and makes the determination required by §219.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.